

X Rays and X Chromosomes

The Leukemia Risk for Girls and Boys

Parents and health care practitioners alike cringe at the mere thought of exposing children to agents associated with cancer. For this reason, the medical world has traditionally shied away from administering prenatal X rays, long known to increase the risk of childhood leukemia. But little research has examined the effects of diagnostic X rays after birth, which are commonly prescribed by doctors. In this issue, a team of Montréal researchers takes a closer look at the underlying interactions between genes and exposure to X rays and concludes that the practice of X-raying youngsters may be putting them at increased risk, as well [EHP 108:495–498].

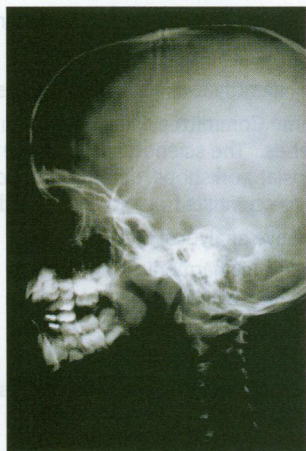
The team, led by McGill University medical professor Claire Infante-Rivard, first explored the link between childhood X rays and the incidence of leukemia by analyzing data collected from telephone interviews with the parents of nearly 1,000 children in Québec, half with documented cases of leukemia. Typically, the children had received mainly bone X rays from ages five to nine. The team found that children who had received two or more X rays after birth were 1.6 times as likely to develop leukemia as children receiving no X rays. The effect was inexplicably more marked among girls: those exposed to two or more X rays more than doubled their risk of leukemia, the team reports.

The researchers probed the link further. In the first-ever effort to describe gene–environment interactions in childhood leukemia, the team examined whether inherited genetic variations, or polymorphisms, influence susceptibility to the disease. Specifically, the team looked at differences in several DNA repair genes among a subgroup of roughly 130 children who were exposed to diagnostic X rays and whose blood had been previously genotyped. They focused on four polymorphisms recently identified in three DNA repair genes.

The team found that these polymorphisms produced effects common to many gene variations; that is, they modulated the risk of children developing leukemia in a manner characteristic of polymorphisms, sometimes increasing the risk, sometimes decreasing it. Moreover, they found that the risks do not necessarily increase with higher exposures to X rays; a girl with a different mutation on a different repair gene, for instance, is actually significantly protected against leukemia upon greater exposure to X rays.

The team also determined that some polymorphisms in DNA repair genes modify risk in girls, while others modify risk in boys. Consider this: among girls, carrying a specific mutation on a repair gene and being exposed to two or more X rays results in a risk of developing leukemia that is over 6.5 times greater than the product of the risk from the mutation and the X-ray exposure. The increased risk reveals a synergistic effect between the polymorphism and exposure to X rays. Meanwhile, a boy with the same mutation and exposure actually has a reduced risk of leukemia.

Overall, the study strongly suggests that the effects of diagnostic radiation after birth may be more striking among girls. And for now, the researchers can't offer a tidy explanation for the gender differences. Infante-Rivard suggests, based on the new findings, that perhaps more



Dangerous diagnostics. The risk of leukemia from exposure to X rays early in life may be greater than previously thought.

caution should be exercised in prescribing X rays for both sexes and more research should be conducted on the actual dosages administered. The study authors also call for more study of polymorphisms in DNA repair genes. —Julie Wakefield

Fetal Attraction

Calcium Can Reduce Effects of Prenatal Lead Exposure

Scientists have long known that much of the lead entering the body during childhood is stored in the skeleton, where it can remain for decades. Most of this skeletal lead is unavailable to target organs (those to which lead is especially toxic) and produces little apparent toxicity during adulthood, although recent studies have found associations between bone lead stores and anemia, hypertension, and other diseases in men. But fractures and a number of conditions including pregnancy can release lead from bone back into the blood. Pregnant women with high skeletal lead concentrations run the risk of exposing their children to lead during critical periods of fetal development.

Dietary calcium has been shown to reduce gastrointestinal absorption of lead and inhibit its adverse effects on calcium-mediated cellular functions. In this issue, Shenggao Han and colleagues from the Department of Preventive Medicine and Community Health at the UMDNJ–New Jersey Medical School in Newark lend further support to the hypothesis that sufficient dietary calcium during pregnancy can reduce the effect of maternal lead stores on fetal development and lead accumulation *in utero* [EHP 108:527–531].

In the study, groups of weanling female rats, five weeks of age, were given drinking water containing 250 milligrams per liter (mg/L) lead acetate for 5 weeks, followed by a 4-week period without lead exposure. Controls were given sodium acetate in drinking water. Both treatment groups and controls were fed diets containing 0.5% calcium. At 14 weeks, the females were mated with male rats of the same age, and the pregnant females were randomly assigned to two groups, one fed a 0.5% calcium diet (normal) and one fed a 0.1% calcium diet (low). Pregnant rats carried their litters to term, and the pups were evaluated for a variety of developmental end points.

Han and colleagues found that pups born to lead-exposed rats were reduced in birth weight and length after controlling for factors such as pup sex, litter size, and maternal weight gain during pregnancy. This is significant because it indicates that lead exposure occurring well before pregnancy can influence fetal development. The results following the rats' exposure at five weeks of age suggest that infants born to women with a history of lead exposure during childhood—the exposure period when the metal can cause the most enduring damage—may experience developmental problems *in utero* as a result.

However, dietary calcium was shown to provide benefits with respect to lead release from bones and fetal uptake. For example, maternal blood lead concentrations were lower in pregnant rats given the higher-calcium diet, which suggests that calcium has an inhibitory effect on lead release from bone. Fetal lead uptake was also reduced in pups born to rats with higher dietary calcium intakes. Dietary calcium did not appear to protect against lead-induced decreases in birth weight and length. Nevertheless, the results of this study provide evidence that the composition of the diet during pregnancy can influence the transfer to the fetus of an environmental toxicant from past maternal exposure. —Charles W. Schmidt

CORRECTION

In the May Science Selections article “Diabetes and Drinking Water” [EHP 108:A225], the citation listed for the original article by van Maanen et al. should have been EHP 108:457–461. EHP regrets the error.